Control of DNA Motion in Microchannels Integrated with Dual Electrodes

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Single molecule analysis is a promising technology for the study of DNA-protein interactions. To perform such studies DNA molecules must be stretched and immobilized at specific locations in a microchannel, and proteins must be introduced at specific locations along the DNA strand without being allowed to widely diffuse. It also may be necessary to mix multiple protein solutions in a controlled fashion to form a complex before DNA interaction. Previous flow studies in microfluidic systems have used streams of a secondary fluid or dielectrophoresis, however, these solutions will not work for focusing of particles in a single fluid, or require the added complexity of electrodes. We have previously developed techniques for the controlled immobilization and stretching of DNA in microchannels using pressure and electrokinetic driven flows and by controlling the properties of surfaces. Here we demonstrate the control of focusing and intermixing of particles in single fluid with a cross-flow configuration by controlling only the channel geometry, as a step toward the development of a system to enable single molecule DNA-protein interaction experiments.

We have fabricated a series of cross-flow microchannels of 500 nm depth, as shown in Fig.1. The vertical channels are 4 μm in width, the horizontal channels vary between 15-60 μm, and the focusing angle varies between 0-70°. To determine the effectiveness of focusing for each channel, we have introduced the flow focus ratio, or ratio of particles which, as traveling horizontally in Fig. 1, traverse straight through the horizontal channel to those that are redirected into the vertical channel. A high ratio means there is little intermixing between particles travelling horizontally and the fluid in the vertical channel, as desired in a DNA-protein interaction study. In the experiments, the system is filled with fluid and fluorescent nanoparticles are driven through the horizontal channel by application of a pressure gradient. The flow focus ratio is determined by counting the number of particles that travel past the cross junction in each direction in an optical microscope, as shown in Fig. 2. We have observed that this ratio is enhanced as the focusing angle is increased, as shown in Fig. 3. Additionally, the flow focus ratio is independent of the average velocity of the nanoparticles, as shown in Fig. 4. The results of Figs. 3 and 4 are supported by finite element simulations. Additionally we are investigating the control of cross-flow focusing and intermixing by variation of the three dimensional geometry (via introduction of a tapered cross-channel), surface properties of the channels, and the introduction of electrodes to allow electrokinetic control of fluid motion. A full single molecule DNA-protein interaction system incorporating DNA stretching, immobilization, and cross-flow focusing is currently under development.

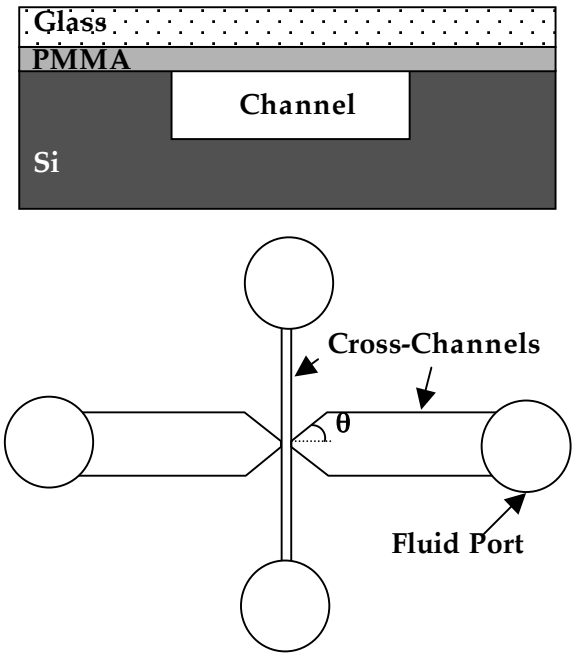

Figure 1: Schematic diagram of cross-section and top view of fluidic channels.

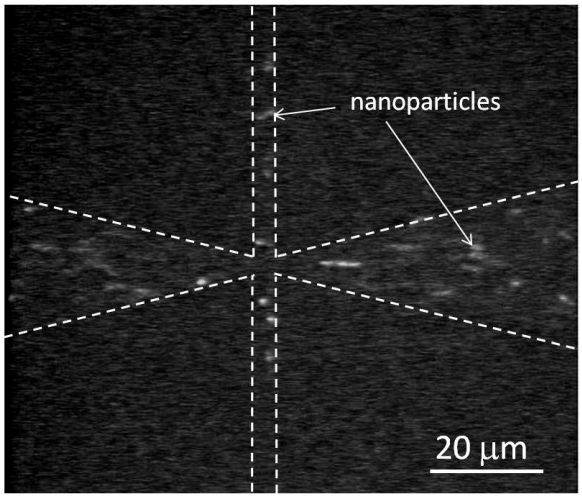

Figure 2: Top-view optical micrograph of 60 μm wide flow focus channel with a focus angle of 14° across 4 μm wide vertical channel. Fluorescent nanoparticles move right to left in the image.

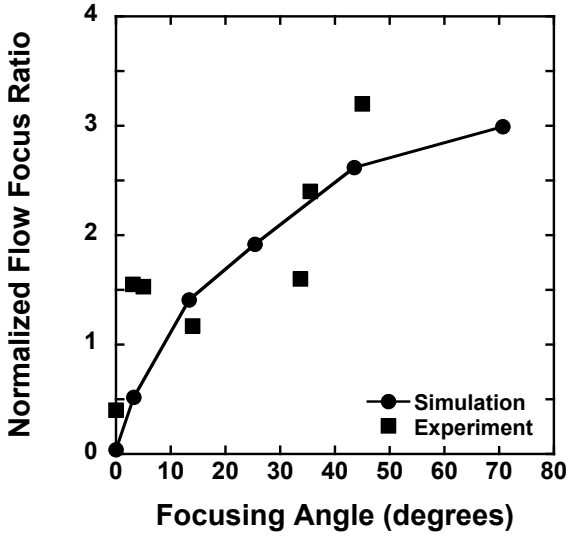

Figure 3: Flow focus ratio as function of focusing angle showing both experimental and simulation results.

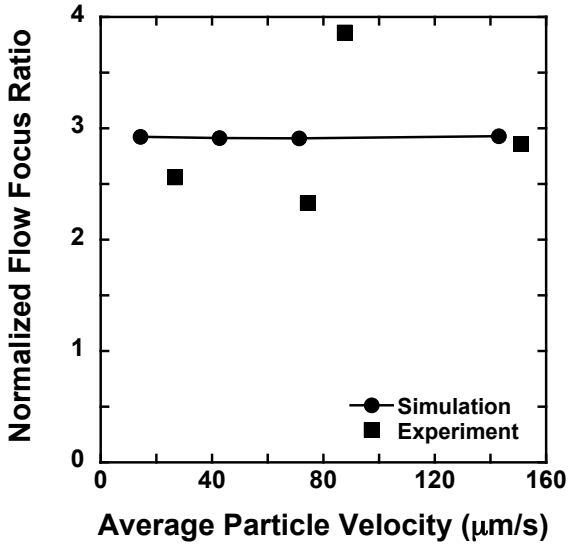

Figure 4: Flow focus ratio as function of nanoparticle velocity showing both experimental and simulation results.